

BRYAN CAVE LEIGHTON PAISNER LLP
THREE EMBARCADERO CENTER, 7TH FLOOR
SAN FRANCISCO, CA 94111-4070

1 K. Lee Marshall (SBN 277092)
2 Abigail Cotton (SBN 306121)
3 BRYAN CAVE LEIGHTON PAISNER LLP
4 Three Embarcadero Center, 7th Floor
5 San Francisco, CA 94111-4078
6 Telephone: (415) 675-3444
7 klmarshall@bclplaw.com
8 abby.cotton@bclplaw.com
9

10 David A. Roodman (appearance *pro hac vice*)
11 Nick E. Williamson (appearance *pro hac vice*)
12 BRYAN CAVE LEIGHTON PAISNER LLP
13 One Metropolitan Square, 36th Floor
14 St. Louis, MO 63102
15 Telephone: (314) 259-2000
16 daroodman@bclplaw.com
17

18 Attorneys for Plaintiffs
19 *Fluidigm Corporation and Fluidigm Canada Inc.*
20

21 UNITED STATES DISTRICT COURT
22
23 NORTHERN DISTRICT OF CALIFORNIA
24
25 SAN FRANCISCO DIVISION
26

27 FLUIDIGM CORPORATION, a Delaware
28 corporation; and FLUIDIGM CANADA INC.,
a foreign corporation,

Plaintiffs,

v.

IONPATH, INC., a Delaware corporation,

Defendant.

Case No. 3:19-cv-05639

**PLAINTIFFS FLUIDIGM
CORPORATION'S & FLUIDIGM
CANADA INC.'S CLAIM
CONSTRUCTION BRIEF**

TABLE OF CONTENTS

Table of Contents	i
Table of Authorities	ii
I. Technology Background.....	1
II. Legal Standards for Claim Construction.	2
III. Claim Construction.....	3
A. “Vaporizing, Atomizing, and Ionizing” - (‘386 & ‘698 Patents).....	3
1. “Vaporization” Does Not Require “Heating.”	4
2. “Vaporization, Atomization, and Ionization” Does Not Require Separate Steps, Much Less Separating Gas Into Atomic Constituents.....	7
B. “Detect,” “Detecting” & “Detected” / “Lanthanides” / “Noble Metals.”	8
1. “Detect,” “Detecting,” “Detected.”	9
2. “Lanthanides.”	9
3. “Noble Metals.”	10
4. IONpath’s Proposed Construction of an “86-Word” Passage.	11
C. “Detecting ... the Elemental Composition of the First/Second Cell.”	12
D. “A First Device” / “A Second Device” - (‘698 Patent).....	13
E. “Detected Sequentially” / “Sequentially Analyzing Single Cells” / “Sequentially Analyzing Single Cells in a Sample.”	17
F. “Transient Signal.”	18
G. “Distinct Isotope.”	19
H. “Pretreating.”	20
Conclusion	21

TABLE OF AUTHORITIES

Cases

<i>3M Innovative Props. Co. v. Tredegar Corp.</i> , 725 F.3d 1315 (Fed. Cir. 2013)	5
<i>GE Lighting Sols., LLC v. AgiLight, Inc.</i> , 750 F.3d 1304 (Fed. Cir. 2014)	5
<i>Greenberg v. Ethicon Endo-Surgery, Inc.</i> , 91 F.3d 1580 (Fed. Cir. 1996).....	16
<i>Honeywell Int’l, Inc. v. ITT Indus., Inc.</i> , 452 F.3d 1312 (Fed. Cir. 2006)	2
<i>Karl Storz Endoscopy-Am., Inc. v. Stryker Corp.</i> , No. C 09-00355 WHA, 2011 WL 1659867 (N.D. Cal. May 3, 2011)	16
<i>Lexion Med., LLC v. Northgate Techs., Inc.</i> , 641 F.3d 1352 (Fed. Cir. 2011)	3
<i>Liebel-Flarsheim Co. v. Medrad, Inc.</i> , 358 F.3d 898 (Fed. Cir. 2004).....	5
<i>Markman v. Westview Instr., Inc.</i> , 517 U.S. 370 (1996).....	2, 3
<i>MTD Prod. Inc. v. Iancu</i> , 933 F.3d 1336 (Fed. Cir. 2019)	14
<i>Oatey Co. v. IPS Corp.</i> , 514 F.3d 1271 (Fed. Cir. 2008).....	8
<i>Personalized Media Commc’ns, LLC v. Int’l Trade Comm’n</i> , 161 F.3d 696 (Fed. Cir. 1998).....	14
<i>Phillips v. AWH Corp.</i> , 415 F.3d 1303 (Fed. Cir. 2005) (<i>en banc</i>)	2, 3, 6, 7
<i>Thorner v. Sony Comput. Entm’t Am. LLC</i> , 669 F.3d 1362 (Fed. Cir. 2012)	5
<i>Vitronics Corp. v. Conceptronic, Inc.</i> , 90 F.3d 1576 (Fed. Cir. 1996)	2
<i>Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.</i> , 853 F.3d 1272 (Fed. Cir. 2017).....	5
<i>WMS Gaming Inc. v. Int’l Game Tech.</i> , 184 F.3d 1339 (Fed. Cir. 1999)	15

Fluidigm Corporation and Fluidigm Canada Inc. (collectively “Fluidigm”) hereby respectfully submit their brief in support of the construction of the disputed terms and limitations of the asserted claims of U.S. Patent Nos. 10,180,386 (the “’386 Patent”) and 10,436,698 (the “’698 Patent”) (collectively, the “Patents”¹). Fluidigm’s constructions are focused on discrete terms, use simple and understandable language, and are rooted in the plain language of the claims and the science of the applicable technology. IONpath’s constructions are focused on lengthy passages, are nearly indecipherable, and are rife with ambiguity and misdirection. The Court should adopt Fluidigm’s proposed constructions.

I. TECHNOLOGY BACKGROUND

The ’386 and ’698 Patents disclose the invention of a new multiplexed analysis of cell samples at the single cell level, using mass spectrometry techniques. (Expert Report of Thomas Kelly (“Kelly Rep.”), ¶ 16). In the multiplexed analysis, a plurality of analytes (such as different proteins or other biomarkers of interest) of the single cells are bound by different tagged antibodies that are each specific for the different analytes. (*Id.*). As each analyte has a different chemical structure, a specific antibody may be selected for that structure, and each particular antibody employed will only bind to that corresponding analyte. (*Id.*).

Each antibody is itself tagged with an elemental tag comprising a lanthanide or noble metal. (*Id.* ¶ 18). The elemental tags thus include an element, or an isotope of an element, that can provide a distinguishable signal for the specific antibody. (*Id.*). The use of elemental tags allows for multiplexing analysis because each tag has a different molecular weight distinguishable by mass spectrometry. (*Id.*). In other words, the protein or biomarker of interest is bound by an antibody which in turn is labeled or tagged with a specific elemental tag. (*Id.*). When the elemental tag is detected by mass spectrometry, it provides a signal indicating that the protein or biomarker of interest was present in or on the cell. (*Id.*).

Importantly, the multiplexed analysis described in the ’386 and ’698 Patents is performed

^{1/} As the ’386 and ’698 Patents share a specification, any citation to the specification of the ’386 Patent should be treated, where appropriate, as including a citation to the corresponding specification of the ’698 Patent (and vice-versa).

by sequential analysis of single cells, such that information about the multiple analytes that may be present in or on different individual cells can be determined at the cellular level. (*Id.* ¶ 19). The sequential analysis of the single cells involves vaporizing, atomizing, and ionizing the multiple elemental tags from each successive cell. (*Id.*). Vaporizing, atomizing, and ionizing is required because the lanthanide or noble metal atoms must be ionized to be detected by mass spectrometry. (*Id.*). By providing for systems and methods that allow for the simultaneous detection of the multiple vaporized, atomized and ionized elemental tags in a transient signal, multiplexed analysis of analytes at the individual cell level is possible.

The ability to evaluate multiplex information at the cellular level has been a transformative breakthrough for medical research, allowing for the identification of interactions and relationships between multiple different proteins or other biomarkers in or on the cells, and providing for the multiplexed profiling of cells to determine correlations between the presence and/or relative levels of multiple different biomarkers and disease states. (*Id.* ¶ 17). Examples of research and/or diagnostic areas where multiplexed single cell analysis technique has been implemented to make new discoveries include, for example, cancer research and immuno-oncology, immunology, immunophenotyping, infectious disease/microbiology studies (including studies on COVID-19), liquid biopsy, neurology, oncology, and stem cell research. (*Id.*).

II. LEGAL STANDARDS FOR CLAIM CONSTRUCTION.

Claim construction is a matter of law and is subject to the familiar standards of *Markman v. Westview Instr., Inc.*, 517 U.S. 370, 373 (1996), and *Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) (*en banc*). The words of the claims are “highly instructive” in determining the meaning of a limitation. *Phillips.*, 415 F.3d at 1314. The claims, however, are not construed in a vacuum. Rather, it is well settled that the claims are construed in light of the specification. *See Honeywell Int’l, Inc. v. ITT Indus., Inc.*, 452 F.3d 1312, 1318 (Fed. Cir. 2006) (“Claims must be read in view of the specification, of which they are a part”); *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996) (“[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.”). The prosecution history of a patent can also provide guidance as to what an

applicant meant by its various terms. *Markman*, 52 F.3d at 980. Together, the claims, specification and prosecution history comprise the “intrinsic evidence,” and are determinative in ascertaining the meaning of claim terms and limitations. *Phillips*, 415 F.3d at 1316-17. “The customary meaning of a claim term is not determined in a vacuum and should be harmonized, to the extent possible, with the intrinsic record, as understood within the technological field of the invention.” *Lexion Med., LLC v. Northgate Techs., Inc.*, 641 F.3d 1352, 1356 (Fed. Cir. 2011). Courts should also look to how the inventor used and defined a term in the specification as “the inventor’s lexicography governs.” *Phillips*, 415 F.3d at 1316.

III. CLAIM CONSTRUCTION.

A. “Vaporizing, Atomizing, and Ionizing” - (‘386 & ‘698 Patents).

A Person of Ordinary Skill in the Art (“POSIA”)² would understand that “vaporizing, atomizing and ionizing” as used in the subject claims means “*generating ionized atomic components from a solid or liquid state of a sample*,” as that is how the term is solely and consistently used in both Patents. (Kelly Rep. ¶ 59). IONpath’s proposed construction (“*to convert the elemental tags to a gas by heating, separating the resulting gas into atomic constituents, and positively or negatively charge these atomic constituents*” (see ECF No. 86-1, Ex. 1 to Joint Claim Construction and Prehearing Statement (“JCC”) at 1) improperly seeks to constrain this term to a particular technique used in a single embodiment and imposes erroneous additional restrictions expressly disavowed by the specification.

A fundamental aspect of the claimed inventions is the need to generate atomic lanthanide or noble metal ions associated with a sample that may be detected and analyzed via mass spectrometry. Specifically, the inventions generate ions from elemental tags (either lanthanide or noble metal atoms) that are attached to antibodies affixed to different analytes in or on cell samples cells. ‘386 Patent, 30:63-65, 31:3-4; ‘698 Patent, 30:62-64; (Kelly Rep. ¶¶ 61-63); *see*

^{2/} A POSIA at the time of the claimed inventions, as of March 25, 2004, would be a person who has: (i) a graduate degree, and preferably a PhD or MD, in a relevant scientific or engineering field (such as materials science, chemistry, physics, materials engineering, medicine, and/or biophysics); and/or (ii) approximately ten (10) years of relevant industry or academic experience relating to mass spectrometry techniques and/or applications thereof. (Kelly Rep. ¶ 55).

also ‘386 Patent, Abstract, 6:51-55, 12:24-27, 13:2-4, 29:62-63. Ions are generated by directing energy into the solid or liquid phase sample to generate ionized atoms from the elemental tags, a method referred to and claimed as “vaporizing, atomizing, and ionizing” multiple elemental tags. (Kelly Rep. ¶¶ 65-66). The resulting ions allow for simultaneous analysis of numerous analytes (known as multiplex analysis) in or on the cells, providing information about the presence of various structures, such as proteins, antigens, and other biomarkers. (Kelly Rep. ¶ 18). The elemental tags are vaporized because they are liberated from the solid or liquid state of the sample. The elemental tags are atomized because the free atoms are separated from the biomolecules to which they were attached. And the elemental tags are ionized because they are charged. There is no specific method or limitation on the method by which the elemental tags are “vaporized, atomized, and ionized” so long as ionized atomic components are generated from a solid or liquid state of a sample. (Kelly Rep. ¶ 63).

IONpath’s proposed construction is, until it injects completely erroneous new limitations, generally consistent with Fluidigm’s construction. In “*convert[ing] the elemental tags ... into atomic constituents, and positively or negatively charg[ing] those atomic constituents*,” IONpath’s construction inherently agrees with Fluidigm’s definition that “vaporization, atomization, and ionization” generates ionized atomic components from a solid or liquid state. (Kelly Rep. ¶ 72). But, in seeking to avoid infringement, IONpath asks the Court to: (1) improperly import an alleged limitation -- “heating” -- that happens to occur in the process described in a single embodiment; (2) require the imposition of a sequenced, three-step, process that is specifically disclaimed in the specification; and (3) add an erroneous limitation that gas must be created and then separated. The Court should reject IONpath’s arguments as contrary to the plain meaning ascribed to the limitation in both Patents.

1. **“Vaporization” Does Not Require “Heating.”**

Nowhere in the Patents, including the claims and specification, is “heat” required to “vaporize, atomize, and ionize” elemental tags. Notwithstanding this fact, IONpath urges the Court to commit a fundamental error by improperly importing a by-product of one embodiment into the claims. *See GE Lighting Sols., LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir.

2014) (“[I]t is improper to read limitations from a preferred embodiment described in the specification—even if it is the only embodiment—into the claims absent a clear indication in the intrinsic record that the patentee intended the claims to be so limited.” (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 913 (Fed. Cir. 2004))). Doing so would be error because: (a) neither the claims nor the specification require heat; (b) the relevant literature expressly recognizes that heat is not required to “vaporize” a sample; (c) the specification describes at least one embodiment able to “vaporize, atomize, and ionize” the elemental tags that does not require heat; and (d) that embodiment — glow discharge — accelerates primary ions at the sample and uses the kinetic energy of those ions to eject or “sputter” material from the sample surface. In this respect, glow discharge uses the same “sputtering” methodology as the SIMS technique that IONpath seeks to artificially exclude from the scope of the claims with a construction requiring “heat.”

First, the claims themselves do not recite “heat.” The specification explains that the requisite ions may be generated using “[a]ny means suitable” to “vaporize, atomize and ionize” the elemental tags – not any particular method or device. ‘386 Patent, 13:2-7, 7:31-41. There is nothing in the specification that would teach a POSIA that the patentees intended to require “heat” to “vaporize, atomize, and ionize,” much less that the limitation be included in the claims. (Kelly Rep. ¶ 73) (“not explicitly or implicitly required by any of the claims”). “[Courts] will not narrow a claim term beyond its plain and ordinary meaning unless there is support for the limitation in the words of the claim, the specification, or the prosecution history.” *Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.*, 853 F.3d 1272, 1281 (Fed. Cir. 2017) (quoting *3M Innovative Props. Co. v. Tredegar Corp.*, 725 F.3d 1315, 1333 (Fed. Cir. 2013)). “[A]bsent a clear disavowal or alternative lexicography by a patentee, he or she ‘is free to choose a broad term and expect to obtain the full scope of its plain and ordinary meaning.’” *Id.* at 1282 (quoting *Thorner v. Sony Comput. Entm’t Am. LLC*, 669 F.3d 1362, 1367 (Fed. Cir. 2012)).

Second, as Dr. Kelly explains, POSIA understood that the term “heat” is not required by the claimed invention. The term “heat” refers to the transfer of energy between two “systems” or macroscopic collectives of atoms. (Kelly Rep. ¶ 73). However, when a material is vaporized at the atomic scale (such as in a glow discharge or SIMS technique), the process is correctly

1 governed by quantum mechanics where the term “heat” is inapplicable. (Kelly Rep. ¶ 73). Even at
2 the system level, the mass spectrometry literature uses the term “vaporize” to refer to a “variety of
3 techniques, including heating the samples, exposing them to a high electric field ... and/or via
4 bombardment with fast atoms, or atomic or molecular ions.” Ex. L to Kelly Rep. (Rubakhin) at 3;
5 *see also id.* (“analytes need to be vaporized from a solid or liquid phase, ionized, and transferred
6 into the vacuum system of the mass analyzer”). IONpath ignores the usage in the relevant field in
7 an attempt to impose an unnecessary limitation on devices used to “vaporize, atomize, and ionize,”
8 when such devices need only employ energy to liberate the ionized atomic components. (Kelly
9 Rep. ¶ 74).

10 Third, the Patents instruct POSIA that any suitable devices may be used to generate ions
11 and identifies no less than four different representative technologies that may be used to vaporize,
12 atomize, and ionize the elemental tags in order to generate the ionized atomic components,
13 namely, glow discharge, graphite furnace, capacitively coupled plasma devices (“CCP”), and
14 inductively coupled plasma (“ICP”). *See, e.g.*, ‘386 Patent, 7:31-41, 13:2-7. There is no teaching
15 that any particular device or process must be read into the claims. *See, e.g., Phillips*, 415 F.3d at
16 1323 (“we have repeatedly warned against confining the claims to” specific embodiments).

17 Ignoring the breadth of the specifications, IONpath attempts to read the term “heat” into
18 the claims by improperly focusing on and misinterpreting *a single embodiment* – ICP – in which a
19 sample is injected into high temperature plasma. But, as Dr. Kelly explains, the temperature of the
20 plasma is simply a means to measure the kinetic energy of excited ions produced by the energized
21 plasma that impacts the sample. (Kelly Rep. ¶ 77). Further, the claimed inventions are not
22 restricted to using ICP, rather, the Patents expressly disclose other methods and POSIA
23 understood alternative devices could be used. *See* ‘386 Patent, 7:31-41, 13:2-7; (Kelly Rep. ¶ 74).
24 At least one of the disclosed methods – glow discharge– does not utilize heat to vaporize a sample.
25 (Kelly Rep. ¶ 78). IONpath’s attempt to restrict this limitation to a single possible method of
26 vaporization that includes heat is a transparent attempt to avoid the clear evidence that
27 vaporization has been used to describe a variety of techniques including the “bombardment with
28 fast atoms, or atomic or molecular ions” that is characteristic of SIMS.

Fourth, and perhaps most telling, is the Patents' identification of "glow discharge" as a technique to "vaporize, atomize, and ionize" elemental tags. '386 Patent, 7:31-34 ("The means to vaporize, atomize and excite or ionize the single particles may include **glow discharge**, graphite furnace, and capacitively coupled plasma devices, or other suitable devices" (emphasis added)). In glow discharge, plasma ions are accelerated towards a sample to be analyzed, with the kinetic energy of the ions being transferred to the sample upon impact, thereby causing surface material to be ejected from the sample surface – a phenomenon referred to as "sputtering." *See* Ex. G to Kelly Rep. (Bogaerts) at 669 ("The use of the glow discharge as an ion source for mass spectrometry is based on the phenomenon of sputtering."); Ex. F to Kelly Rep. (Blades) at 16A ("The impinging ion ... penetrates to a depth of a few angstroms where its kinetic energy can cause surface atoms to be ejected ... a phenomenon called sputtering."). As a side note, "sputtering" via SIMS (which is what the accused product employs) necessarily involves transfer of at least some heat to the sample, as excess primary ion energy will end up in atomic vibrations in the sample ("heat") as a by-product. (Kelly Rep. ¶ 83).

There is no basis to import a "heating" limitation into the claims. The claims and specifications do not require "heating," POSIA would not understand the claims to require "heating," and it would be error to insert such a limitation as, among other things, it would also exclude a disclosed embodiment. *See Phillips*, 415 F.3d at 1323 (POSIA "rarely would confine their definitions of terms to the exact representations depicted in the embodiments").

2. **"Vaporization, Atomization, and Ionization" Does Not Require Separate Steps, Much Less Separating Gas Into Atomic Constituents.**

In addition to its erroneous "heating" limitation, IONpath seeks to impose a three-step sequence, including an unsupported intermediate step of separating gas into atomic constituents. None of these limiting embellishments are required by the claims or specification – rather, the Patents expressly teach the opposite.

As the Patents teach, and a POSIA understood at the time, "vaporization, atomization, and ionization" can occur simultaneously. Notably, in at least one of the exemplary techniques identified in the Patents, "glow discharge," vaporization and atomization occurs simultaneously,

not in sequence.^{3/} (Kelly Rep. ¶¶ 86-87). Also, the Patents state that vaporization, atomization, and ionization can, in some instances occur in different devices and at different times, meaning that in other instances it occurs at the same time/in the same device. ‘386 Patent, 13:7-9 (“in some instances, vaporization, atomization, and ionization ... can occur in different devices and at different times”). IONpath’s attempt to have the Court require a “three-step” process runs directly afoul of the claims and specification, improperly eliminating one of the preferred devices disclosed in the Patents. *See Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1277 (Fed. Cir. 2008) (“[W]here claims can reasonably be interpreted to include a specific embodiment, it is incorrect to construe the claims to exclude that embodiment, absent probative evidence on the contrary.”).

B. “Detect,” “Detecting” & “Detected” / “Lanthanides” / “Noble Metals.”

Fluidigm provides constructions for all of these specific claim terms. IONpath oddly does not. Instead, IONpath asks the Court to construe a portion of Claim 1 of the ‘698 Patent under 35 U.S.C. § 112(6) (discussed *infra*), then also asks the Court to construe 86 words of that portion of Claim 1 of the ‘698 Patent, while refusing to provide constructions for the individual claim terms:^{4/}

<p>“a second device to detect, by mass spectrometry, lanthanides and/or noble metals of the single first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single first cell, and lanthanides and/or noble metals of the single second cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single second cell, wherein the transient signal associated with the single</p>	<p>“detect . . . lanthanides and/or noble metals of the single first cell . . . , and lanthanides and/or noble metals of the single second cell”</p> <p>IONpath Proposed Construction: “individually discerning on a cell-by-cell basis . . . the lanthanides and/or noble metals that make up the first cell . . . individually discerning on a cell-by-cell basis . . . the lanthanides and/or noble</p>
---	--

^{3/} Further, IONpath’s attempt to insert an intermediate “gaseous” step is not supported by the claims or specification. A POSIA would not equate the word “vaporization” with the word “gas,” as “gas” is not required for the generation of the vaporized and ionized atomic components.” (Kelly Rep. ¶ 85). The Patents teach and claim that what is critical is that the elemental tags are broken down or atomized to liberate the ionized atomic components to permit mass-differentiation between different tags. (*Id.*). IONpath’s proposed construction invites error.

^{4/} IONpath ignores the individual claim terms on page 10 of Exhibit 1 to the Joint Claim Construction Statement, but does elect to provide a consolidated proposed construction for “lanthanides” and “noble metals” later on page 25 of the Exhibit. ECF No. 86-1, Ex. 1 to JCC at 10, 25.

first cell and the transient signal associated with the single second cell are detected sequentially.”

IONpath Proposed Construction:
This term is governed by § 112(6)

ECF No. 86-1, Ex. 1 to JCC at 6.

metals that make up the second cell”

ECF No. 86-1, Ex. 1 to JCC at 10.

Fluidigm respectfully submits that IONpath’s proposal is flawed and inappropriate.

1. “Detect,” “Detecting,” “Detected.”

Both the ‘386 and ‘698 Patents, and independent Claim 1 of both Patents, use the terms “detect,” “detecting,” “detected,” in their plain and ordinary manner. The Patents do not use these common terms in any peculiar manner, and do not impose any new or different meanings. As such, the Court should construe each of these terms to have their plain and ordinary meaning. (Kelly Rep. ¶ 130).

2. “Lanthanides.”

The ‘698 Patent also uses the common term “lanthanides” that is understood by a POSIA to mean “any element having atomic numbers 57-71.” (Kelly Rep. ¶ 135). While IONpath ignores this term in connection with its proposed construction for “detect ... lanthanides and/or noble metals of the single first cell ... , and lanthanides and/or noble metals of the single second cell ... ,” it appears to generally agree with Fluidigm’s construction of “lanthanide.” Regrettably, however, IONpath ties its proposed construction to a flawed definition of “noble metals.” ECF No. 86-1, Ex. 1 to JCC at 25. As “lanthanides” and “noble metals” are separate terms, they should be defined separately (and correctly). Fluidigm’s construction of “lanthanides” (“*any element having atomic numbers 57-71*”) is consistent with both the scientific meaning of the term and also the express definition that these same inventors used in their prior patent application that was made of record during prosecution. (Kelly Rep. ¶ 136); *see also* ‘698 Patent, 1:17-23 (incorporating U.S. Patent App. 09/905,907 (the “907 App”)).

IONpath’s apparent construction also vaguely broadens the set of lanthanides by claiming “compositions comprising element (sic) with atomic number 57-71.” To the extent IONpath is arguing for a construction that would allow the detection of lanthanide-containing structures larger

than the lanthanide elements, such a construction would be at cross-purposes with the stated objectives of the Patents to distinguish between different lanthanides and/or noble metals themselves, functioning as elemental tags. (Kelly Rep. ¶ 139).

3. “Noble Metals.”

Similarly, the ‘698 Patent uses the term “noble metals” that is understood by POSIA to mean:

“Noble metals include any of several metallic elements, the electrochemical potential of which is much more positive than the potential of the standard hydrogen electrode, therefore, an element that resists oxidation. Examples include palladium, silver, iridium, platinum, and gold.”

(Kelly Rep. ¶ 135). This definition is copied verbatim from another patent application filed by the inventors of the Patents, which application was wholly incorporated by reference in the Patents. *See* ‘698 Patent, 1:17-23 (incorporating by reference the ‘907 App); (Kelly Rep. ¶ 137). As stated above, IONpath improperly ties the two definitions for lanthanides and noble metals together, and argues that they include:

“element, isotope, ion, and/or composition comprising element with atomic number 57-71, ruthenium, rhodium, palladium, silver, indium, hafnium, rhenium, iridium, platinum, gold, ruthenium (sic), copper, osmium, mercury, or nickel.”

ECF No. 86-1, Ex. 1 to JCC at 25.

While some of the non-lanthanide elements listed by IONpath are correctly identified as noble metals, others would not be so characterized by a POSIA. For example, indium and nickel are all elements that a POSIA would not identify as noble metals. (Kelly Rep. ¶ 117). Furthermore, copper has an electrochemical potential that is much lower than the noble metals palladium, silver, iridium, platinum and gold that are referred to in the intrinsic record. (Kelly Rep. ¶ 140). IONpath’s proposed construction is also inconsistent with the disclosures of the Patents, which specify that the elemental tags selected for use with the invention are those that are “not[e] expected to be common in biological systems,” (‘698 Patent, 10:6-8), which would exclude copper and nickel elements. (Kelly Rep. ¶ 140). IONpath’s proposed construction includes elements that are not noble metals as well as elements that a POSIA would understand are not appropriate for their intended purpose. IONpath’s construction also has the same issues with overinclusion of “composition[s]” that plague its proposed construction for lanthanides and fails for the same

reason. (Kelly Rep. ¶ 140; *see also id.*, ¶ 139). For these reasons, IONpath’s proposed construction should be rejected.

4. IONpath’s Proposed Construction of an “86-Word” Passage.

IONpath propounds the following construction for the “86-word” passage:

“individually discerning on a cell-by-cell basis ...the lanthanides and/or noble metals that make up the first cell...individually discerning on a cell-by-cell basis ... the lanthanides and/or noble metals that make up the second cell.”

ECF No. 86-1, Ex. 1 to JCC at 10. The Court should reject the construction of such an unwieldy passage comprised of multiple elements and limitations. Additionally, IONpath uses the camouflage of this long construction to inject and import new limitations into the claim: “the lanthanides and/or noble metals that make up the first [and second] cell,” and “discerning on a cell-by-cell basis.” *Id.* At best, IONpath’s construction introduces improper ambiguity, and, at worst, injects inapplicable limitations by requiring that: (1) lanthanides and/or noble metals “make up” a cell, which is scientifically and factually wrong; and (2) “all” elements of a cell must be detected -- not just the ionized elements of the elemental tags. (Kelly Rep. ¶ 112-114; *see also id.*, ¶ 107-109).

First, IONpath’s inclusion of the limitation -- “the lanthanides and/or noble metals that make up the first [and second] cell” is fatally deficient as it erroneously requires that a cell be “made up” of lanthanides and/or noble metals. Yet, as the ‘698 Patent explains and a POSIA would understand, the cells of interest are not “made up” of lanthanides or noble metals, rather, lanthanides and noble metals are tags which are attached to antibodies which bind to biomarkers in or on cells of interest. ‘698 Patent, Claim 1, 30:57-62. Indeed, the lanthanides and noble metals were selected as tags precisely because they are not endogenous to most cells. (Kelly Rep. ¶¶ 112-114; *see also id.*, ¶¶ 107-109). IONpath propounds a construction that simply makes no sense.

Second, neither the claims nor specification require that all elements that “make up” a cell be detected. Tellingly, if IONpath is seeking a construction so it may argue that this passage requires that all endogenous elements must be detected, the construction would erroneously contradict and teach away from what is claimed and taught throughout the ‘698 Patent – namely, the detection of the elemental tags indicating the presence of specific, sought-after biomarkers, not

1 necessarily the identification of every element in the cell. The claims and patent teach and require
 2 only that the transient signals from vaporized, atomized, and ionized elemental tags are detected.
 3 ‘698 Patent, 30:66 - 31:9 (“detecting a transient signal of the multiple vaporized, atomized, and
 4 ionized elemental tags of the single first cell”). As a POSIA would understand, if the limitations
 5 were improperly interpreted to require that all elements of a cell be detected, it would require the
 6 absurd and impossible result of the detection of every element of every molecule contained in or
 7 on a cell. (Kelly Rep. ¶ 109-111). No POSIA would construe the claims, passage, limitations, or
 8 Patents in this manner. (Kelly Rep. ¶ 111).

9 **C. “Detecting ... the Elemental Composition of the First/Second Cell.”**

10 The parties identified specific “detecting” limitations in the ‘386 Patent for construction,
 11 namely: “detecting, using mass spectrometry, the elemental composition of the first [and second]
 12 cell.” ECF No. 86-1, Ex. 1 to JCC at 12-14.

13 Fluidigm’s proper construction of these limitations is:

14 *“analyzing elements or isotopes of the elemental tags bound to analyte in or on the first*
 15 *cell [and second cell], by mass spectrometry.”*

16 (Kelly Rep. ¶ 102). The meaning of the claim limitations is clear from the claim itself, and is
 17 entirely consistent with the specification. The limitations require using mass spectrometry to
 18 detect and analyze the elemental tags that were bound to analytes of the cells. ‘386 Patent, 2:55-65
 19 (*e.g.*, “analyze the elemental composition of the vaporized, atomized, ionized... particles, or an
 20 elemental tag associated with the particles”); 5:52-67 (“A tag can include for example an element
 21 or isotope of an element that is associated with an analyte or analyte complex and which is
 22 measured to determine the presence of the analyte”); 6:7-18 (“analysis of particles ... by
 23 measuring ... a tag or label associated with an analyte located on or in the cell”) ; 7:47-61 (“The
 24 elemental composition of the particle or elemental tag is determined by a spectrometer ...”);
 25 30:66-31:12. (Kelly Rep. ¶ 103-104). Fluidigm’s construction is consistent with the intrinsic
 26 evidence.

27 IONpath, on the other hand, asks the Court to attach erroneous and ambiguous restrictions
 28 to its construction:

1 *“individually discerning on a cell-by-cell basis” ... the elements that make up the first*
 2 *cell.”*

3 IONpath’s strategy of trying to add two inapplicable limitations (“discerning on a cell-by-cell
 4 basis” and “the elements that make up the first cell”) injects improper requirements that have no
 5 bases in the Patents, and injects ambiguity where there should be none.

6 Neither claim limitation includes IONpath’s proposed addition of “individually discerning
 7 on a cell-by-cell basis” “the elements that make up the first cell.” Importantly, the claims and
 8 subject limitations are clearly directed to only detecting transient signals associated with ionized
 9 elemental tags to determine information regarding targeted analytes – not the elements that “make
 10 up the first cell,” much less all of the elements that “make up the first cell.” *See, e.g.*, ‘386 Patent,
 11 30:55 – 31:12 (“a sample containing a plurality of tagged cells tagged with a plurality of tagged
 12 antibodies, wherein each of the tagged antibodies is specific for a different analyte”; “detecting a
 13 transient signal of the multiple vaporized, atomized, and ionized elemental tags of the first cell”);
 14 (Kelly Rep. ¶¶ 110-111). IONpath’s new limitations are made up out of whole cloth, are not
 15 within the scope of the claim, and appear to be intended to require that an accused method
 16 “discern[] ... the elements that make up” a cell, which is neither claimed nor taught by the ‘386
 17 Patent. (*Id.*). Further, the claims and specification cannot fairly, or otherwise, be interpreted to
 18 suggest that all endogenous elements be detected, which would be impossible. (*Id.*). IONpath’s
 19 construction should be rejected.

20 **D. “A First Device” / “A Second Device” - (‘698 Patent).**

21 Claim 1 of the ‘698 Patent includes the term “a first device” to “vaporize, atomize, and
 22 ionize” multiple elemental tags, as taught by the Patents, and “a second device” to detect, by mass
 23 spectrometry, transient signals produced by the first device. ‘698 Patent, 30:62 - 31:6. Both of
 24 these terms should be deemed to have their plain and ordinary meaning.

25 A POSIA at the time would understand that the claimed “first device” to “vaporize,
 26 atomize, and ionize” can be any “suitable” device to “vaporize, atomize and ionize” the elemental
 27 tags, of which there are numerous such devices. ‘386 Patent, 13:2-7, 7:31-41; (Kelly Rep. ¶¶ 90-
 28 91) (*e.g.* glow discharge, SIMS, graphite furnace, CCP, and ICP). There is no reason or basis to

1 restrict the term to any specific device.

2 IONpath argues, instead, that this term is subject to 35 U.S.C. § 112(6), that the term “first
3 device” is a “means,” and the corresponding structure is limited to one of four representative
4 pieces of equipment referenced in the Patents (glow discharge, graphite furnace, CCP, and ICP),
5 and “equivalents thereof,” that must have a specific input configuration, *in combination with* a
6 separate, distinct, injection system device. IONpath’s construction is flawed.

7 Initially, as the limitation, a “first device to vaporize, atomize, and ionize multiple
8 elemental tags” lacks the term “means,” there is a presumption that it is not subject to § 112(6).
9 *Personalized Media Commc’ns, LLC v. Int’l Trade Comm’n*, 161 F.3d 696, 703-04 (Fed. Cir.
10 1998) (“[T]he word ‘means’ creates a presumption that § 112, ¶ 6 applies, and ... the failure to use
11 the word ‘means’ creates a presumption that § 112, ¶ 6 does not apply,” (citations omitted)). The
12 standard for determining whether § 112(6) applies is whether the words of the claim are
13 understood by a POSIA to have a “sufficiently definite meaning as the name for the structure.”
14 *MTD Prod. Inc. v. Iancu*, 933 F.3d 1336, 1341 (Fed. Cir. 2019). Here, the limitation provides
15 sufficient detail for a POSIA at the time to understand what common and ordinary devices fall
16 within its scope. As Dr. Kelly explains, a POSIA would understand from the claim itself that the
17 “first device to vaporize, atomize, and ionize multiple elemental tags” encompasses glow
18 discharge, graphite furnace, ICP, CCP, SIMS, other ion beam devices, microwave induced plasma,
19 DC-glow discharge, RF-glow discharge, spark source, laser ablation/ionization, electrospray,
20 capacitive microwave plasma, and direct current plasma. (Kelly Rep. ¶ 91). Dr. Kelly also
21 explains that the fact that the ‘698 Patent expressly describes vaporizing, atomizing, and ionizing
22 multiple elemental tags, and then employing time-of-flight mass spectrometry to detect and
23 analyze the ions, expressly teaches and discloses to a POSIA that the claimed “first device to
24 vaporize, atomize, and ionize” encompasses pulsed types of ion generating devices such as SIMS
25 and laser ablation. (*Id.*). In 2004, POSIA understood that creating ions employing SIMS and laser
26 ablation provided the level of precision necessary to determine when an ion left a sample to
27 accurately measure time of flight for mass spectrometry purposes. (Kelly Rep. ¶ 92); *see also*,

1 ‘386 Patent (Abstract; Col. 1, 18-20; Claim 17; Claim 19).⁵

2 Second, even if, *arguendo*, the Court were to conclude that there is insufficient structure in
3 the claim and that § 112(6) is applicable, IONpath spuriously tries to fold in a unique input
4 configuration based on an *entirely separate* device used to introduce samples -- sheath flow
5 injection systems:

6 “A glow discharge, graphite furnace, capacitively coupled plasma device, or inductively
7 coupled plasma (ICP) device, **with an input configured to receive the output of a cell or
8 particle injector systems in use for flow cytometry, including sheath flow injection
systems, and equivalents thereof.**”

9 ECF No. 86-1, Ex. 1 to JCC at 4 (emphasis added).

10 This is a clear invitation for error. The Patents are unambiguous that equipment before the
11 claimed “first device to vaporize, atomize, and ionize,” including “sample introduction systems,”
12 are *separate* devices. ‘698 Patent, 11:50-53 (“The sample introduction system 102 can comprise
13 several devices that are currently in use with other flow cytometry sample introduction systems”);
14 11:63-67 (“All sample introduction devices suitable for the purposes disclosed herein; including
15 ICP devices, will serve, regardless of whether they now exist or are hereafter developed or
16 improved.”); 6:8-12 (“particles that have been introduced into a device to vaporize, atomize and
17 excite or ionize them”). The claimed “first device to vaporize, atomize, and ionize” does not and
18 cannot encompass equipment (entirely different “devices”) used to feed samples into the “first
19 device to vaporize, atomize, and ionize.” Nor can a specific input configuration be required for
20 the “first device to vaporize, atomize, and ionize,” as Claim 1 and the ‘698 Patent make clear that
21 the “first device” does not include or encompass a “sample introduction system” and, further, the
22 specification explains that POSIA understood that several different devices were available that
23 could be used at the time, and that the invention was not restricted to any specific construction.
24 ‘698 Patent, 11:53-55, 63-67.

25 This fundamental disconnect is clearly illustrated by IONpath’s own proposed

26 ^{5/} Importantly, even if § 112(6) is found to apply, the scope of the first device includes all of
27 the devices and equipment disclosed to POSIA in the ‘698 Patent (glow discharge, graphite
28 furnace, CCP, ICP, and other suitable devices), and, necessarily, “equivalents thereof” that
perform the same function of vaporizing, atomizing, and ionizing multiple elemental tags. *See*,
e.g., *WMS Gaming Inc. v. Int’l Game Tech.*, 184 F.3d 1339, 1351 (Fed. Cir. 1999).

1 construction. IONpath identifies the function of the alleged § 112(6) term as: “to vaporize,
2 atomize, and ionize multiple elemental tags from a single first cell of the plurality of tagged cells
3 and multiple elemental tags from a single second cell of the plurality of tagged cells.” But
4 IONpath’ subsequent claimed structure recites structures that are wholly unrelated to the asserted
5 function. Structure unrelated to the claimed function has no place in a means-plus-function
6 construction. *See, e.g., Karl Storz Endoscopy-Am., Inc. v. Stryker Corp.*, No. C 09-00355 WHA,
7 2011 WL 1659867, at *11-12 (N.D. Cal. May 3, 2011) (dismissing a proposed construction
8 because it attempts to add structure with an unrelated function).

9 As for the claimed “second device,” Claim 1 specifically identifies the device as a mass
10 spectrometer of any type: “a second device to detect, by mass spectrometry.” (Kelly Rep. ¶ 93). A
11 POSIA at the time, including Dr. Kelly, would understand that the ‘698 Patent teaches and
12 discloses that the “second device” is a mass spectrometer: a common and ordinary instrument used
13 by scientists at the time to detect transient signals. (*Id.*). Further, there can be no legitimate
14 dispute that the claim includes sufficient structure, specifically identifying a mass spectrometer,
15 such that it is not subject to § 112(6). *See Greenberg v. Ethicon Endo-Surgery, Inc.*, 91 F.3d 1580,
16 1583 (Fed. Cir. 1996) (“[T]he fact that a particular mechanism is defined in functional terms is not
17 sufficient to convert a claim element containing that term into a ‘means for performing a specified
18 function’ within the meaning of section 112(6). Many devices take their names from the functions
19 they perform.”). As Dr. Kelly affirms, POSIA at the time regularly employed common mass
20 spectrometry technology to detect transient signals. (Kelly Rep. ¶ 93). The fact that the
21 specification provides exemplary alternative types of mass spectrometry instrumentation does not
22 mean that Claim 1 fails to identify sufficient structure to perform mass spectrometry. Indeed, if
23 anything, it makes it clear that Claim 1 provides sufficient structure, as POSIA at the time
24 understood that the specific type of device includes a mass spectrometer, ToF MS, simultaneous
25 or sequential mass analyzers, array-detector magnetic sector, 3D ion trap, linear ion trap,
26 quadrupole devices, and equivalents thereof. (*Id.*); *see also* ‘698 Patent 17:66-18:3, 18:6-23.

E. “Detected Sequentially” / “Sequentially Analyzing Single Cells” / “Sequentially Analyzing Single Cells in a Sample.”

Claim 1 of the ‘386 and ‘698 Patents both provide that the “transient signal associated with the first cell and the transient signal associated with the second cell are detected sequentially” – with the exception that the ‘698 Patent adds the word “single” in front of the terms “first cell” and “second cell.” ‘386 Patent, 31:9-12; ‘698 Patent, 31:6-9 (emphasis added).

Fluidigm submits that the proper construction of “detected sequentially,” as would be understood by a POSIA, is:

“observed at separate times.”

(Kelly Rep. ¶ 116). The claims and specifications of the Patents fully support this construction as they consistently describe the analysis being performed at different times, as opposed to performing an analysis on two or more cells at the same time. (*Id.* ¶¶ 117-119).

Despite the fact that “detected sequentially” is a stand-alone limitation at the end of both claims (the last two words of each claim), IONpath fails to provide any construction for “detected sequentially.” ECF No. 86-1, Ex. 1 to JCC at 15. Instead, IONpath provides proposed constructions for phrases in the respective, *non-binding*, preambles of the claims, namely: “sequentially analyzing single cells” and “sequentially analyzing single cells in a sample.”^{6/} *Id.* at 15-20. If the Court finds that the preamble language are limiting, Fluidigm states that the terms should be given the following constructions, as would be understood by a POSIA:

- “Sequentially analyzing single cells”: *“analyzing single cells at separate times”;*
- “Sequentially analyzing single cells in a sample”: *“analyzing single cells in a sample separately, not at the same time.”*

(Kelly Rep. ¶¶ 116, 120).

Although IONpath advocates constructions for non-limiting preambles, just as it encourages the Court to import new and unsupported limitation into “Detecting ... the Elemental Composition of the First/Second Cell,” it likewise seeks to inject the unsupported limitations

^{6/} While the preambles are non-limiting, Fluidigm proposed a provisional construction in the event the Court were to find the phrase limiting.

1 *composition and cell-by-cell* into “sequentially analyzing single cells [in a sample].”^{7/} In doing so,
 2 IONpath propounds the unsupported definition: “*individually discerning elemental composition on*
 3 *a cell-by-cell basis.*” ECF No. 86-1, Ex. 1 to JCC at 15, 18.

4 While IONpath argues that “sequentially” must be “understood in the context of the
 5 surrounding language,” (ECF No. 86-1, Ex. 1 to JCC at 15), it then proceeds to wholly ignore that
 6 very language. *Id.* at 15, 18. Both claims expressly provide that:

7 “a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the
 8 [single] first cell,” and “a transient signal of the multiple vaporized, atomized, and ionized
 9 elemental tags of the [single] second cell,” are “detected sequentially.” ‘386 Patent, 31:7-
 12; ‘698 Patent, 31:4-9 (“single” added for Claim 1 of the ‘698 Patent).

10 As the claims make clear, it is the signals from the ionized elemental tags that are detected.
 11 The limitations are expressly directed to detecting and analyzing transient signals associated with
 12 ionized elemental tags, and the analytes to which they correspond – not the “elemental
 13 composition” of each of the cells. Stated in another way, the claims are directed to, as POSIA
 14 understand, detecting signals that correspond to specific analytes on or in cells – not every element
 15 that might be present in or on a cell. (Kelly Rep. ¶¶ 110-111). IONpath’s construction, intentional
 16 or not, is manifestly incorrect.

17 **F. “Transient Signal.”**

18 The asserted claims of both Patents recite the term “transient signal.” The common
 19 meaning of the term “transient” is “lasting only for a short time” or “passing especially quickly
 20 into and out of existence.” Similarly, the meaning of the word “signal” as used in the Patents is
 21 detectable ionized components of elemental tags after vaporization, atomization, and ionization.
 22 *See, e.g.*, ‘386 Patent, 5:52-59, 9:47-52, 17:21-38. As such, Fluidigm states that the proper
 23 construction of “transient signal,” as would be understood by a POSIA, is:

24 “*The detectable ions generated for a limited duration of time.*”

25 (Kelly Rep. ¶ 128). Fluidigm’s construction is properly founded upon the claims, specifications,
 26 and prosecution histories of the patents-in-suit, as well as what POSIA understand.

27 _____
 28 ^{7/} IONpath does not appear to contest Fluidigm’s construction, rather, IONpath attempts to
 add unsupported additional limitations.

1 The Patents and claims are directed to mass spectrometry-based multi-parametric particle
 2 analysis which detects “transient signals” of ionized components of elemental tags that have a
 3 duration of microseconds, for example, “last for a period in the range of 20 to 200 microseconds.”
 4 ‘386 Patent, 18:8-10; (Kelly Rep. ¶ 128). The prosecution histories, likewise, reference the fact
 5 that the signals generated from detectable ions are of limited duration in time. Ex. D to Kelly Rep.
 6 (Sept. 18, 2018 Amendment) at 8; (Kelly Rep. ¶ 129).

7 IONpath fails to provide a construction for “transient signal.” Instead, again,
 8 IONpath improperly seeks to construe the following entire passages, this time 22 words for the
 9 ‘386 Patent (actually the combination of two passages), and 24 words for the ‘698 Patent:

10 “detecting ... wherein the transient signal associated with the first cell and the transient
 11 signal associated with the second cell are detected sequentially.” ‘386 Patent, 30:66-31:2,
 31:6-12.

12 “detecting ... wherein the transient signal associated with the single first cell and the
 13 transient signal associated with the single second cell are detected sequentially.” ‘698
 Patent, 31:1-9.

14 ECF No. 86-1, Ex. 1 to JCC at 21-23. IONpath proposes the following identical construction for
 15 both of these passages:

- 16 • “detecting the individual signal of an individual cell event for the first cell, and
 17 detecting the individual signal of an individual cell event for the second cell.”

18 *Id.* Not only is the definition IONpath propounds silent on the meaning of “transient signal,” its
 19 proposed use of the terms “individual signals” and “individual cell event” for the first cell and
 20 second cell are undefined and inject ambiguity. For example, if IONpath’s use of “individual cell
 21 event” refers to the vaporization, atomization, and ionization of an elemental tag from a cell, and
 22 its reference to “individual signal” corresponds to detectable ions of limited duration associated
 23 with the ionized elemental tag, then its definition is similar to Fluidigm’s construction. (Kelly Rep.
 24 ¶ 133). However, as such terms lack a clear definition, IONpath’s proposed construction is vague,
 25 ambiguous, and improper.

26 **G. “Distinct Isotope.”**

27 A POSIA at the time would understand that the term “distinct isotope,” as used in the
 28 subject claims, specification, and file history, means:

1 *“an isotope of an element that has a distinguishable mass from other isotopes, of the*
 2 *same or other element, used as tags in that sample.”*

3 Kelly Rep. ¶¶ 141-142. The Patents are directed to multiplex analysis of cell samples (the
 4 ability to simultaneously identify multiple different analytes in a cell sample) by using elemental
 5 tags that act as labels for different analytes and provide a distinguishable signal indicating the
 6 presence of an analyte or analyte complex with which each elemental tag is associated. *See, e.g.,*
 7 ‘386 Patent, 5:52-67. The elemental tags in turn contain an element, or an isotope of an element,
 8 that provides the distinguishable signal. ‘386 Patent, 5:52-67 (“the tag (which is also called an
 9 ‘elemental tag’) can contain an element or an isotope ... that provide[s] the distinguishable
 10 signal”).

11 Specifically, in Claim 1 of each of the Patents, the elemental tags comprise “a lanthanide
 12 or noble metal,” which can include distinct isotopes, and are used to tag antibodies specific for
 13 different analyte in the sample. The Patents teach that multiplexing can be achieved by using
 14 distinct isotopes of elements, where the distinct isotopes each have a distinguishable mass from
 15 other isotopes, of the same or other element, used as tags. *See, e.g.,* ‘386 Patent, 5:52-67. Distinct
 16 isotopes can comprise isotopes of the same or other elements, as long as the masses of the isotopes
 17 used to tag each antibody are distinguishable from one another to allow for separate identification
 18 by mass spectrometry. (Kelly Rep. ¶¶ 144-145).

19 **H. “Pretreating.”**

20 “Pretreating the multiple vaporized, atomized and ionized elemental tags of the first cell
 21 occurs in a vacuum,” as used in the claims, specification, and file history of the ‘386 Patent means:
 22 *“conditioning a group of element tag ions in a vacuum and transporting to the mass*
 spectrometer.”

23 The patent describes exemplary ion pretreatment systems that transport ions generated by
 24 the vaporization, atomization and ionization process to, and which may condition ions for, the
 25 mass analyzer. ‘386 Patent, 3:18-30; 14: 7-11. For example, the patents describes preferred
 26 embodiments having a pretreatment devices that condition ions for time-of-flight mass
 27 spectrometers, and/or filter ions. ‘386 Patent, 7:10-14, 8:7-10. As such, a POSIA at the time
 28 would understand “pretreating the multiple vaporized, atomized and ionized elemental tags of the

1 first cell occurs in a vacuum,” as used in Claim 18 of the '386 Patent, to mean “*conditioning a*
2 *group of element tag ions in a vacuum and transporting to the mass spectrometer.*” (Kelly Rep.
3 ¶¶ 148-150).

4
5 **CONCLUSION**

6 Fluidigm respectfully requests the Court adopts its proposed constructions, which are
7 focused on discrete terms, are easily understandable, are based on the plain language, and are
8 consistent with the intrinsic and extrinsic evidence.

1 Dated: July 16, 2020

2 By: /s/ Abigail Cotton

3 K. Lee Marshall (SBN 277092)
4 Abigail Cotton (SBN 306121)
5 BRYAN CAVE LEIGHTON PAISNER LLP
6 Three Embarcadero Center, 7th Floor
7 San Francisco, CA 94111-4078
8 Telephone: (415) 675-3444
9 klmarshall@bclplaw.com
10 abby.cotton@bclplaw.com

11 David A. Roodman (appearance *pro hac vice*)
12 Nick E. Williamson (appearance *pro hac vice*)
13 BRYAN CAVE LEIGHTON PAISNER LLP
14 One Metropolitan Square, 36th Floor
15 St. Louis, MO 63102
16 Telephone: (314) 259-2000
17 daroodman@bclplaw.com

18 *Attorneys for Plaintiffs*
19 *Fluidigm Corporation and Fluidigm Canada Inc.*
20
21
22
23
24
25
26
27
28

CERTIFICATE OF SERVICE

I hereby certify that on July 16, 2020, I electronically filed the above document with the Clerk of the Court using CM/ECF which will send electronic notification of such filing to all registered counsel.

Dated: July 16, 2020

By: /s/ Abigail Cotton